

We Claim:

1. A modified gp120 polypeptide comprising portions of at least two conserved regions of an envelope protein selected from a primate lentivirus, wherein at least one of the following changes relative to the wild-type to gp120 protein is made:

- (a) introduction of disulfide bonds;
- (b) filling a cavity of the gp120 protein with hydrophobic amino acid residues;
- (c) introducing a Pro residue at a defined turn structure; or
- (d) increasing the hydrophobicity across the interface between the gp120 domains,

wherein the modified polypeptide maintains the overall 3-dimensional structure of a discontinuous conserved epitope of the wild-type gp120.

2. The modified gp120 polypeptide of claim 1, wherein the discontinuous conserved epitope is a CD4BS epitope or CD4i epitope.

3. The modified gp120 polypeptide of claim 2, wherein the gp120 protein is selected from the group consisting of HIV-1, HIV-2 and SIV.

4. The modified gp120 polypeptide of claim 3, wherein the gp120 protein is HIV-1.

5. The modified gp120 polypeptide of claim 4, wherein disulfide bonds are introduced between at least one of the groups of amino acids that correspond to Pro118-Ala443, Leu122-Gly431, Phe210-Gly30, or Ser256-Phe376 of the HIV-1 HXBc2 strain.

6. The modified gp120 polypeptide of claims 4 or 5, wherein at least one amino acid residue corresponding to wild-type gp120 Ser375, Val255, Arg273, Ser481, Ser447, Asn377 of the HIV-1 HXBc2 strain, Thr283, or Asp477 of the HIV-1 HXBc2 strain, has been substituted with a hydrophobic amino acid residue.

7. The modified gp120 polypeptide of claim 6, wherein at least one of the following amino acid substitutions is present:

Trp for Ser375, Val255 or Arg 273;

Phe for Ser481;

Ile for Ser447 or Thr283;

or Leu for Asn377 or Thr283.

DRAFT DRAFT DRAFT

- 59 -

8. The modified gp120 polypeptide of claim 6, wherein a Pro residue has been introduced at a defined turn structure.
9. The modified gp120 polypeptide of claim 5, wherein a Pro residue has been introduced at a defined turn structure.
10. The modified gp120 polypeptide of claim 4, wherein a Pro residue has been introduced at a defined turn structure.
11. The modified gp120 polypeptide of claim 8, wherein a Pro residue has been substituted for Ile423.
12. The modified gp120 polypeptide of claim 9, wherein a Pro residue has been substituted for Ile423.
13. The modified gp120 polypeptide of claim 10, wherein Pro has been substituted for Ile423.
14. The modified gp120 polypeptide of claim 1, wherein at least two of the changes have been made,
15. The modified gp120 polypeptide of claim 14, wherein the discontinuous conceived epitope is selected from the group of epitopes consisting of CD4i, CD4BS, and 2G12 epitopes.
16. The modified gp120 polypeptide of claim 15, wherein at least three of the changes have been made.